

## REMARKS

The present paper is filed in response to a final office action dated November 12, 2010. A response is due on May 12, 2011 by virtue of the attached petition and fee for a three-month extension of time to respond. This response also is accompanied by the fee and a request for continued examination.

### A. Status of Claims

Claims 97, 157-175, 177-182 and 184-188 are pending and under examination. The claims remain rejected under 35 U.S.C. 103(a) as allegedly being obvious in view of a variety of combination of references. Applicants respectfully traverse the rejection.

The Examiner noted that the previous arguments were not commensurate in scope with the claims because the arguments relied in some part on the arrays being comprised of different oligonucleotides but claims 181 and 186 did not require such arrays to contain different identities of oligonucleotides. Applicants have amended claims 181 and 186 to expressly recite that each array comprises oligonucleotides of different sequences attached thereto. As such Applicants believe the claims are commensurate in scope with the non-obviousness arguments advanced.

As noted by the applicants previously, the primary reference of Southern is acknowledged as not teaching any methods or means of keeping separated the arrays and probes in corresponding arrays and this lack of teaching cannot be remedied by the teachings of either Kauver or Wang. Kauver is related to producing a more sensitive measurement of a single analyte, which in the case of Kauver is methyl mannose, a small molecule that binds to Concanavalin A (a lectin). In contrast, the array of arrays of the

present invention is one that is used to identify different analytes – where the different analytes (oligonucleotide) have distinct chemical structures. Figure 3 of Southern merely shows an arrangement of 4 arrays of oligonucleotides but each array is identical in terms of the oligonucleotides that are attached to each array so that replicate measurements of the same reaction are taken. In this way the parallel use of all 4 arrays in the same hybridization reaction conditions is made possible but parallel use in different hybridization reactions, e.g., using different labeled probes for the hybridization reactions in individual unit arrays on a single support cannot be achieved because the arrays of Southern lack separation of the unit arrays and hence any attempt to perform such multiple reactions on the Southern array would not be effective because the reaction mixture from one array would bleed into another and obscure the results obtained. The skilled person would not be motivated to combine Kauver with Southern because Kauver is directed at increasing the sensitivity of binding of a single sugar moiety of known structure to a lectin. This is a different endeavor than Southern. Kauver relates to detecting a known entity (the sugar) using a known binding agent (concanavalin A). Kauver has nothing to do with determining the structure of the methyl mannose. Indeed, concanavalin A as a lectin may bind to one of many different sugars. Southern on the other hand is concerned with sequencing (i.e., determining the structure of) a target nucleic acid sequence of unknown structure by determining which known counterpart nucleic acid the unknown target sequence binds to. The binding only happens where there is complementarity between the target sequence and the oligonucleotide probe. These are two different technical fields of endeavor and the mere fact that Kauver asserts that it has an interest in region-specific signal detection for “convenience and simplicity of interpreting results” does not overcome the fact that Kauver

already knows the identity of the thing being detected and the method of Kauver provides no structural information about the mannose detected.

Wang again is simply related to creating a matrix with a barrier pad in it that is impregnated with hydrophobic material. There is nothing in Wang that shows why doing so would lead to a better hybridization array of Southern. Southern adequately achieved sequencing of a small target nucleic acid in a particular type of sequencing by hybridization reaction. Use of the four arrays was, as noted by the examiner, to increase region specific signal detection using the same reaction conditions for all four arrays. Southern was not concerned with needing to perform multiple hybridization reactions using different sets of probes on the same array and hence Southern did not require separation of the arrays. Indeed, separating the arrays of Southern would have created an impediment or delay in the assay in that same reaction mixture would have to be supplied in four steps to the four separate arrays.

The combination of Drmanac with the remaining references also does not render obvious the presently claimed invention. The Drmanac reference relates to sequencing a target nucleic acid wherein the target nucleic acid is immobilized on the substrate. The detection in Drmanac is achieved by adding labeled probes to the immobilized target. The fact that the probes are not immobilized in the Drmanac reference means that the need for separation of the different areas of the substrate is not necessary because the different areas of the substrate are all coated with the same molecule of one structure i.e., the target that is to be sequenced. Given that there is no need to separate the different areas of the target bound substrate there would be no reason for the skilled person to modify the Drmanac reference with teachings that show hydrophobic or other separation barriers.

In view of the amendment to the claims and the above remarks Applicants believe the rejection should be withdrawn and respectfully request reconsideration of the claims for allowance

The Commissioner is authorized to charge any additional fees or credit any overpayment to the Deposit Account of McAndrews, Held & Malloy, Account No. 13-0017.

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Respectfully submitted,

/Nabeela R. McMillian, #43,363/

Nabeela R. McMillian

Reg. No. 43,363

McAndrews, Held & Malloy, Ltd.  
500 West Madison Street  
34<sup>th</sup> Floor  
Chicago, IL 60661  
Telephone: (312) 775-8000  
Facsimile: (312) 775-8100